REMARKS

The first paragraph of the Specification has been amended to update the status of an application from which this application claims priority.

Response to Restriction Requirement – Group I Election with Partial Traverse

The Office Action first requires restriction to one of three inventions. Applicants elect the Group I claims 31-35 and 53-55 "drawn to an MN antisense construct that comprises antisense oligonucleotide sequence complementary to SEQ ID NO: 5 or SEQ ID NO: 1. . . ." [Office Action, page 2.] Applicants reserve the right under 35 USC Section 121 to file subsequent divisional application(s) to protect the invention commensurate with the scope as originally filed.

The Office Action then requires further restriction of Group I, stating at pages 5-7:

> [T]he antisense sequences listed in claims 31, 33 and 55 are subject to restriction. . . .
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> Claims 31, 33 and 55 are subject to an additional restriction since the nucleotide sequences claimed are not considered to be a proper genus/Markush. . . . If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction. **Since the decisions in In re Weber, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) an In re Haas, . . . 198 USPQ 334 (CCPA (1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention.** In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984).

> **Broadly, unity of invention exists where compounds included with a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.**
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> Claims 31 and 33 specifically claim antisense oligonucleotides that are complementary to SEQ ID NO: 5 and 1, respectively wherein those sequences can be one of SEQ ID NO: 3, 4, or 7, as listed in claim 55. In the instant case, although the antisense sequences claimed each target and modulate expression of MN gene, the instant antisense sequences are considered to be unrelated, since each antisense sequence claimed is structurally and functionally independent and distinct for the following reasons: each antisense sequence has a unique nucleotide sequence, each antisense sequence targets a different and specific region of an MN nucleic acid, and absent evidence to the contrary, each antisense, upon binding to an MN nucleic acid, is expected to functionally modulate **(increase or decrease)** the expression of MN to varying degrees. As such the Markush/genus of antisense nucleotide sequences in claims 31, 33 and 55 are not considered to constitute a proper genus, and are therefore subject to restriction.
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> . . . .
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> In view of the foregoing, one (1) antisense sequence is considered to be a reasonable number of sequences for examination. Accordingly, applicant is required to elect either one (1) antisense sequence from claim 55 that that corresponds with a target nucleotide sequence that is SEQ ID NO: 5 or SEQ ID NO: 1, from claims 31 and 33, respectively. Note that this is not a species election.

[Emphasis added.] Applicants respectfully traverse the secondary requirement for further restriction of the Group I claims but provisionally elect SEQ ID NO: 3. Applicants respectfully request reconsideration and withdrawal of the said secondary restriction requirement in view of the following.

Applicants first respectfully defer to the Manual of Patent Examining Procedures [MPEP] § 1434 entitled "Examination of Patent Applications Claiming Large Numbers of Nucleotide Sequences" which states:

> Nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141. In establishing the new policy, **the Commissioner has partially waived the requirements of 37 CFR 1.141 and will permit a reasonable number of such nucleotide sequences to be claimed in a single application. Under this policy, in most cases, up to 10 independent and distinct nucleotide sequences will be examined in a single application without restriction. Those sequences which are patentably indistinct from the sequences selected by the applicant will also be examined. *Nucleotide sequences encoding the same protein are not considered to be independent and distinct and will continue to be examined together.***

[Emphasis added.] Applicants respectfully point out that SEQ ID NOS: 3, 4 and 7 could be interpreted under MPEP § 2434 **not** "to be independent and distinct" as each of the subject SEQ ID NOS essentially encode the same protein, that is, an MN polypeptide. Should SEQ ID NOS: 3, 4 and 7 **not** be considered "independent and distinct," said sequences should "continue to be examined together . . . " in accordance with MPEP § 2434.

SEQ ID NO: 1 is a partial MN cDNA having 1399 base pairs (bps) and is part of SEQ ID NO: 5 which provides the full-length MN cDNA having 1522 bps. SEQ ID NOS: 3, 4 and 7 are antisense nucleotide sequences that are complementary to SEQ ID NO: 1 as shown in Figure 1A-B. SEQ ID NO: 3 is a 29-mer that is complementary to positions 44-72 of Figure 1A-B (as indicated in the application at page 119, lines 5-7). SEQ ID NO: 4 is a 19-mer that is complementary to positions 12-

30 of Figure 1A-B (as indicated at page 119, lines 8-9). SEQ ID NO: 7 is a 25-mer that is complementary to positions 242-266 of Figure 1A-B.

Applicants respectfully point out that MPEP § 2434 also indicates that the Commissioner

> will permit a reasonable number of such nucleotide sequences to be claimed in a single application. **Under this policy, in most cases, up to 10 independent and distinct nucleotide sequences will be examine in a single application without restriction.**

[Emphasis added.] Even if the subject 3 antisense nucleotide sequences were considered to be "independent and distinct," why would not the Commissioner's policy be applied to the instant situation wherein only 3 sequences are involved, when under the policy "in most cases, up to 10 independent and distinct nucleotide sequences will be examined in a single application without restriction"?

Applicants respectfully regard the claimed antisense constructs as their invention, and claim 55 as a proper Markush claim in accordance with the series of Court of Customs and Patent Appeals (CCPA)[1] decisions (cited in the Office Action) culminating in the case of In re Harnisch, 206 USPQ 300 (CCPA 1980). The examination of Markush claims is governed by MPEP § 803, which is based on that series of CCPA cases and provides an exception to the normal practice of requiring restriction or election.

The CCPA in In re Harnisch (id.) specifically states that in many cases Markush claims do include inventions which would otherwise be considered

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1. The CCPA is a predecessor court to the Court of Appeals for the federal Circuit. In the Federal Circuit's first reported opinion, South Corp. v. United States, 215 USPQ 657 (Fed. Cir. 1982), the Federal Circuit adopted as binding precedent "the holdings of our predecessor courts, the United States Court of Claims and

independent and distinct [MPEP § 803.02]. Applicants then respectfully submit that whether the subject SEQ ID NOS are patentably distinct or not, if there is unity of invention, then the elements of a Markush claim should be examined in one application.

Applicants respectfully argue that SEQ ID NOS: 3, 4 and 7 constitute a proper Markush group as they share a common utility, which utility is set forth in claim 31 as "antisense activity" as demonstrated in the in vitro screening assay outlined in claim 31, wherein "if MN expression is decreased, that said MN antisense construct shows antisense activity." The Office Action refers at page 6 to "each antisense, upon binding to an MN nucleic acid, is expected to functionally modulate **(increase or decrease)** the expression of MN to varying degrees." [Emphasis added.] However, as claim 31 makes clear, the antisense oligonucleotides of the subject claims are those that only **decrease** MN expression. SEQ ID NOS: 3, 4 and 7 then have the common utility of decreasing MN expression. SEQ ID NOS: 3, 4 and 7 further "share a substantial structural feature disclosed as being essential to that utility . . . " [Office Action, page 5], that is, each is an MN antisense oligonucleotide that is complementary to the MN cDNA; that structural feature of the 3 nucleotide sequences being MN antisense sequences complementary to the MN cDNA, is essential to their common utility of decreasing MN expression. Applicants respectfully conclude that SEQ ID NOS: 3, 4 and 7 constitute a proper Markush group.

Applicants further respectfully submit that examination of the Group I claims in their full scope should not be an undue burden on the Examiner in that MN antisense nucleotide sequences, including the specific MN antisense sequences, SEQ ID NOS: 3, 4 and 7, have already been examined by the PTO and found patentable.

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the United States Court of Customs and Patent Appeals [CCPA]. . . ."

Zavada et al., U.S. Patent No. 6,069,242 claims compositions comprising MN antisense nucleic acids and a pharmaceutically acceptable carrier. Claim 8 of that '242 patent claims such a composition "wherein said oligonucleotide is selected from the group consisting of SEQ ID NOS: 3, 4 and 7." Zavada et al., U.S. Patent No. 6,774, 117 B1 claims methods of treating preneoplastic/neoplastic disease associated with abnormal MN gene expression comprising administering a MN antisense oligonucleotide that is complementary to SEQ ID NO: 5. Claim 4 of the '117 patent refers to the method of claim 1 "wherein said MN antisense oligonucleotide is selected from the group consisting of SEQ ID NOS: 3, 4 and 7."

Applicants respectfully request reconsideration of the subject secondary restriction requirement in view of the above remarks, case law, MPEP sections and Commissioner's policy, and withdrawal of the secondary restriction.

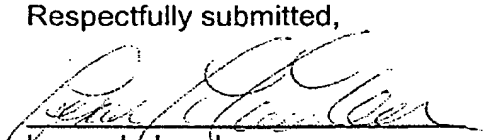
CONCLUSION

As explained above, Applicants respectfully conclude that the subject Restriction Requirement to the extent it requires a further restriction of the Group I claims is mistaken. Applicants respectfully request reconsideration and withdrawal of the secondary restriction requirement and examination of the Group I claims without further restriction.

If the Examiner should consider that a telephone conference could be helpful to address any issues raised by the subject response or could expedite the

prosecution of the subject application, the Examiner is invited to telephone the undersigned Attorney for the Applicant at (415) 981-2034.

Respectfully submitted,



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